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=> s 120014-06-4
L1            1 120014-06-4
                (120014-06-4/RN)

=> d

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   120014-06-4  REGISTRY
ED   Entered STN:  07 Apr 1989
CN   1H-Inden-1-one, 2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-
     piperidinyl]methyl]-  (CA INDEX NAME)
OTHER NAMES:
CN   (±)-E 2020
CN   1-Benzyl-4-[(5,6-dimethoxy-1-oxoindan-2-yl)methyl]piperidine
CN   Donepezil
DR   142057-79-2
MF   C24 H29 N O3
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, CSNB, DDFU, DRUGU,
       EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, MSDS-OHS,
       PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER,
       USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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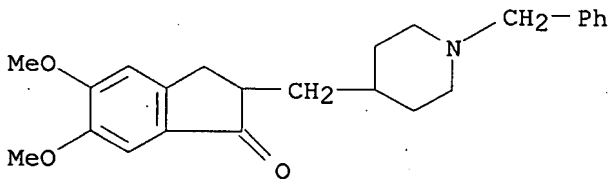


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             18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            809 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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L2          809 L1

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        683339 RESIDUE?
        279150 AMORPH?
        271237 SPRAY?
        472863 DRY
        414750 DRIED
         12909 SPRAY?(3W)(DRY OR DRIED)
L3          11 L2 AND (NONCRYSTAL? OR RESIDUE? OR AMORPH? OR (SPRAY?(3W)(DRY
               OR DRIED)))

=> d bib abs hit 11

L3   ANSWER 11 OF 11  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   1989:173102  CAPLUS
DN   110:173102
TI   Preparation of 1-benzyl-4-(substituted alkyl)piperidines and analogs as
     acetylcholinesterase inhibitors
IN   Sugimoto, Hachiro; Tsuchiya, Yutaka; Higurashi, Kunizou; Karibe, Norio;
     Iimura, Yuoichi; Sasaki, Atsushi; Yamanashi, Yoshiharu; Ogura, Hiroo;
     Araki, Shin; et al.
PA   Eisai Co., Ltd., Japan
SO   Eur. Pat. Appl., 103 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
FAN.CNT 1
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 296560	A2	19881228	EP 1988-109924	19880622
	EP 296560	A3	19900502		
	EP 296560	B1	19960228		
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	FI 8802716	A	19881223	FI 1988-2716	19880608
	FI 95572	B	19951115		
	FI 95572	C	19960226		
	NO 8802696	A	19881223	NO 1988-2696	19880617
	NO 177590	B	19950710		
	NO 177590	C	19951018		
	ZA 8804338	A	19890329	ZA 1988-4338	19880617
	US 4895841	A	19900123	US 1988-209339	19880620
	DK 8803379	A	19881223	DK 1988-3379	19880621
	DK 172337	B1	19980330		
	HU 50768	A2	19900328	HU 1988-3160	19880621
	HU 214592	B	19980428		
	DD 283377	A5	19901010	DD 1988-316988	19880621
	RU 2009128	C1	19940315	RU 1988-4356030	19880621

	CA 1338808	C	19961224	CA 1988-569944	19880621
	AU 8818216	A	19881222	AU 1988-18216	19880622
	AU 627151	B2	19920820		
	CN 1030752	A	19890201	CN 1988-103779	19880622
	CN 1024547	B	19940518		
	JP 01079151	A	19890324	JP 1988-153852	19880622
	JP 2578475	B2	19970205		
	EP 579263	A1	19940119	EP 1993-113146	19880622
	EP 579263	B1	19980916		
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	EP 673927	A1	19950927	EP 1995-104080	19880622
	EP 673927	B1	20010919		
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	AT 134618	T	19960315	AT 1988-109924	19880622
	ES 2083359	T3	19960416	ES 1988-109924	19880622
	EP 742207	A1	19961113	EP 1996-110252	19880622
	EP 742207	B1	20010829		
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	ES 2121039	T3	19981116	ES 1993-113146	19880622
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	AT 205828	T	20011015	AT 1995-104080	19880622
	ES 2160747	T3	20011116	ES 1996-110252	19880622
	ES 2164720	T3	20020301	ES 1995-104080	19880622
	US 5100901	A	19920331	US 1989-423349	19891018
	CN 1073939	A	19930707	CN 1992-112982	19921110
	CN 1034015	B	19970212		
	CN 1071417	A	19930428	CN 1992-112995	19921112
	CN 1038839	B	19980624		
	JP 07252216	A	19951003	JP 1994-291169	19941125
	JP 2733203	B2	19980330		
	CA 1340192	C	19981215	CA 1995-616996	19950424
	FI 9502850	A	19950609	FI 1995-2850	19950609
	FI 102534	B	19981231		
	FI 102534	B1	19981231		
	FI 9602753	A	19960704	FI 1996-2753	19960704
	FI 103969	B	19991029		
	FI 103969	B1	19991029		
	DK 9601082	A	19961003	DK 1996-1082	19961003
	DK 175246	B1	20040719		
	DK 9601083	A	19961003	DK 1996-1083	19961003
	DK 175717	B1	20050131		
	JP 10067739	A	19980310	JP 1997-186306	19970711
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	GR 3036553	T3	20011231	GR 2001-401406	20010906
PRAI	JP 1987-155058	A	19870622		
	FI 1988-2716	A	19880608		
	US 1988-209339	A3	19880620		
	CA 1988-569944	A3	19880621		
	CN 1988-103779	A	19880622		
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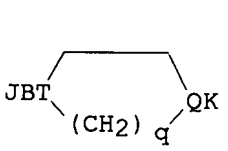
GI					



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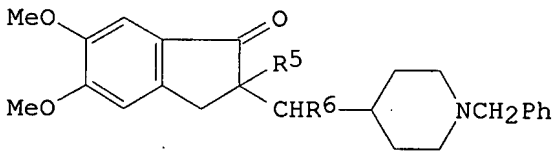

III

AB The title compds. [I; B = (CHR2)r, CO(CHR2)r, NR4(CHR2)r, etc.; J = alkyl, cyclic amide residue, R1CH:CH, (un)substituted Ph, cyclohexyl, heterocyclyl, mono- or divalent (un)substituted indanyl, PhCOCHMe, etc.; K = H, acyl, (un)substituted Ph, aralkyl, etc.; Q = N, C (sic), NO; R1 = H, alkoxycarbonyl; R2 = H, Me; R4 = H, alkyl, acyl, (un)substituted Ph; PhCH2, etc.; T = N, C; q = 1-3; r = 0-10; JB and BT may be doubly bonded] were prepared Ph3PCH2OMeCl was stirred 30 min at 0° with BuLi in Et2O after which 1-benzyl-4-piperidone was added and the mixture stirred at room temperature 3 h to give an oil which was refluxed 3 h in aqueous MeOH containing HCl to give 1-benzylpiperidine-4-carboxaldehyde (II). 5,6-Dimethoxy-1-indanone was stirred with (Me2CH)2NLi in THF containing HMPA after which II was added and the mixture stirred 2 h to give indanonylidenemethylpiperidine III (R5R6 = bond) which was hydrogenated over Pd/C to give, after acidification, III.HCl (R5 = R6 = H). The latter gave 55% inhibition of scopolamine-induced learning impairment in rats at 0.125 mg/kg orally.

AB The title compds. [I; B = (CHR2)r, CO(CHR2)r, NR4(CHR2)r, etc.; J = alkyl, cyclic amide residue, R1CH:CH, (un)substituted Ph, cyclohexyl, heterocyclyl, mono- or divalent (un)substituted indanyl, PhCOCHMe, etc.; K = H, acyl, (un)substituted Ph, aralkyl, etc.; Q = N, C (sic), NO; R1 = H, alkoxycarbonyl; R2 = H, Me; R4 = H, alkyl, acyl, (un)substituted Ph; PhCH2, etc.; T = N, C; q = 1-3; r = 0-10; JB and BT may be doubly bonded] were prepared Ph3PCH2OMeCl was stirred 30 min at 0° with BuLi in Et2O after which 1-benzyl-4-piperidone was added and the mixture stirred at room temperature 3 h to give an oil which was refluxed 3 h in aqueous MeOH containing HCl to give 1-benzylpiperidine-4-carboxaldehyde (II). 5,6-Dimethoxy-1-indanone was stirred with (Me2CH)2NLi in THF containing HMPA after which II was added and the mixture stirred 2 h to give indanonylidenemethylpiperidine III (R5R6 = bond) which was hydrogenated over Pd/C to give, after acidification, III.HCl (R5 = R6 = H). The latter gave 55% inhibition of scopolamine-induced learning impairment in rats at 0.125 mg/kg orally.

IT 120014-06-4P 120014-07-5P 120014-08-6P 120014-09-7P
120014-10-0P 120014-11-1P 120014-12-2P 120014-13-3P 120014-14-4P
120014-15-5P 120014-16-6P 120028-72-0P 120028-73-1P 120028-74-2P
120028-75-3P 120028-76-4P 120028-77-5P 120028-78-6P 120028-79-7P
121202-92-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as acetylcholinesterase inhibitor)

=> d bib hit 10

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:861473 CAPLUS
DN 134:32972
TI Porous drug matrixes containing polymers and sugars and methods of their manufacture
IN Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg
PA Acusphere, Inc., USA
SO PCT Int. Appl., 45 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072827	A2	20001207	WO 2000-US14578	20000525
	WO 2000072827	A3	20010125		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6395300	B1	20020528	US 1999-433486	19991104
	CA 2371836	A1	20001207	CA 2000-2371836	20000525
	CA 2371836	C	20060131		
	EP 1180020	A2	20020220	EP 2000-939365	20000525
	EP 1180020	B1	20051214		
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	BR 2000010984	A	20020430	BR 2000-10984	20000525
	JP 2003500438	T	20030107	JP 2000-620939	20000525
	NZ 516083	A	20030829	NZ 2000-516083	20000525
	AU 768022	B2	20031127	AU 2000-54459	20000525
	AT 312601	T	20051215	AT 2000-939365	20000525
	EP 1642572	A1	20060405	EP 2005-27194	20000525
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	ES 2250141	T3	20060416	ES 2000-939365	20000525
	CN 1823737	A	20060830	CN 2005-10136940	20000525
	US 2002041896	A1	20020411	US 2001-798824	20010302
	US 6610317	B2	20030826		
	NO 2001005753	A	20020128	NO 2001-5753	20011126
	MX 2001PA12106	A	20030630	MX 2001-PA12106	20011126
	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
	HK 1048956	A1	20060728	HK 2003-101310	20030220
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		
	US 1999-433486	A	19991104		
	US 2000-186310P	P	20000302		
	CN 2000-808161	A3	20000525		
	EP 2000-939365	A3	20000525		
	WO 2000-US14578	W	20000525		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a

preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 50-99-7, Dextrose, biological studies 52-53-9, Verapamil 53-03-2, Prednisone 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 67-97-0D, Vitamin D3, analogs 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 745-65-3, Alprostadil 846-49-1, Lorazepam 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 30516-87-1, Zidovudine 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 59729-33-8, Citalopram 60142-96-3, Gabapentin 60205-81-4, Ipratropium 63659-18-7, Betaxolol 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1, Alendronate 66852-54-8, Halobetasol propionate 69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 85721-33-1,

Ciprofloxacin 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 91161-71-6, Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2, Risperidone 106463-17-6, Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6, Zafirlukast 109889-09-0, Granisetron 110871-86-8, Sparfloxacin 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate 112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan 114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil 124832-26-4, Valacyclovir 127779-20-8, Saquinavir 131918-61-1, Paricalcitol 132539-06-1, Olanzapine 134308-13-7, Tolcapone 134678-17-4, Lamivudine 137862-53-4, Valsartan 140678-14-4, Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride 143011-72-7, Granulocyte colony-stimulating factor 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 147059-72-1, Trovafloxacin 147245-92-9, Glatiramer acetate 150378-17-9, Indinavir 154248-97-2, Imiglucerase 154598-52-4, Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir 158966-92-8, Montelukast 159989-65-8, Nelfinavir mesylate 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib 171599-83-0, Sildenafil citrate 679809-58-6, Enoxaparin sodium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for
enhancement of drug dissoln.)

=> d bib hit 9

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:716930 CAPLUS
DN 136:33811
TI Synthesis and Screening for Antiacetylcholinesterase Activity of (1-Benzyl-4-oxopiperidin-3-ylidene)methylindoles and -pyrroles Related to Donepezil
AU Andreani, Aldo; Cavalli, Andrea; Granaiola, Massimiliano; Guardigli, Massimo; Leoni, Alberto; Locatelli, Alessandra; Morigi, Rita; Rambaldi, Mirella; Recanatini, Maurizio; Roda, Aldo
CS Dipartimento di Scienze Farmaceutiche, Universita di Bologna, Bologna, 40126, Italy
SO Journal of Medicinal Chemistry (2001), 44(23), 4011-4014
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:33811
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The design, synthesis, and rapid evaluation of a new class of acetylcholinesterase (AChE) inhibitors related to donepezil are reported. A mol. dynamics simulation of the complex between AChE and one representative compound of the series showed a possible inhibitor binding mode in which favorable interactions are formed between the benzylpiperidinone moiety and some active-site residues. The

biochem. evaluation of this newly synthesized series was performed using a chemiluminescent method suitable for high-throughput screening.

IT 9000-81-1, Acetylcholinesterase 120014-06-4, Donepezil
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and screening for antiacetylcholinesterase activity of (1-benzyl-4-oxopiperidin-3-ylidene)methylindoles and -pyrroles related to donepezil)

=> d bib hit 8

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:816444 CAPLUS
DN 135:352829
TI Combination therapeutic compositions containing benzene compounds
IN Jaen, Juan C.; Chen, Jin-Long
PA Tularik Inc., USA
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001082916	A2	20011108	WO 2001-US14393	20010502
	WO 2001082916	A3	20020704		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002037928	A1	20020328	US 2001-847887	20010502
	US 6653332	B2	20031125		
	US 2004259918	A1	20041223	US 2003-456932	20030605
	US 2006035928	A1	20060216	US 2005-258817	20051026
PRAI	US 2000-201613P	P	20000503		
	US 2001-847887	A1	20010502		
	US 2003-456932	A1	20030605		

OS MARPAT 135:352829
AB The present invention provides pharmaceutical compns. and methods for the treatment of diabetes mellitus using combination therapy. The compns. relate to a benzene compound and an antidiabetic agent such as sulfonylureas, biguanides, glitazones, α-glucosidase inhibitors, potassium channel antagonists, aldose reductase inhibitors, glucagon antagonists, activators of RXR, insulin therapy or other anti-obesity agent. The methods include the administration of the combination of benzene compound with antidiabetic agent where the two components are delivered in a simultaneous manner, where the benzene compound is administered first, followed by the antidiabetic agent, as well as wherein the antidiabetic agent is delivered first followed by the benzene compound For example, the benzene compound (I) was synthesized using a 5-amino-2-(3-chloro-5-pyridyloxy)benzonitrile (0.457 g) in methylene chloride to which was added 2,4-dichlorobenzenesulfonyl chloride (0.456 g), followed by pyridine (150 μL). The reaction progress was monitored by TLC, and upon completion the solvent was removed under vacuum. The resulting residue was partitioned between methylene chloride and water. The organic layer was drawn off and concentrated The residue was triturated with ether to provide 0.447 g of I as a white solid, m.p.

154-156°.

IT 50-18-0, Cyclophosphamide 50-78-2, Aspirin 52-53-9, Verapamil 53-03-2, Prednisone 53-86-1, Indomethacin 55-63-0, Nitroglycerin 56-03-1D, Biguanide, derivs. 59-05-2, Methotrexate 59-67-6, Niacin, biological studies 64-77-7, Tolbutamide 64-86-8, Colchicine 86-54-4, Hydralazine 94-20-2, Chlorpropamide 114-07-8, Erythromycin 114-86-3, Phenformin 124-94-7, Triamcinolone 154-93-8, Carmustine 300-62-9, Amphetamine 315-30-0, Allopurinol 339-44-6, Glymidine 451-71-8, Glyhexamide 518-28-5, Podophyllotoxin 525-66-6, Propranolol 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1406-18-4, Vitamin E 3149-00-6, Phenbutamide 4205-90-7, Clonidine 4759-48-2, Isotretinoin 5581-42-0, Glyparamide 5588-38-5, Tolpyrramide 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 10540-29-1, Tamoxifen 13010-20-3D, Nitrosourea, metal derivs. 13598-36-2D, Phosphonic acid, alkylidenebis- derivs. 15663-27-1, Cisplatin 19216-56-9, Prazocine 21187-98-4, Gliclazide 23214-92-8, Doxorubicin 24455-58-1, Glicetanile 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 33069-62-4, Paclitaxel 33342-05-1, Gliquidone 33419-42-0, Etoposide 35273-88-2, Gliflumide 42399-41-7, Diltiazem 45086-03-1, Etoformin 50925-79-6, Colestipol 51876-98-3, Gliamilide 56180-94-0, Acarbose 59865-13-3, Cyclosporine 62571-86-2, Captopril 72432-03-2, Miglitol 74772-77-3, Ciglitazone 79902-63-9, Simvastatin 80879-63-6, Emiglitate 83480-29-9, Voglibose 93479-97-1, Glimepiride 97322-87-7, Troglitazone 103787-97-9, BM 131246 103788-05-2, AD-5075 104343-33-1, MDL-25637 104987-11-3, FK-506 106650-56-0, Sibutramine 109229-58-5, Englitazone 111025-46-8, Pioglitazone 114798-26-4, Losartan 120014-06-4, Donepezil 122320-73-4, Rosiglitazone 127214-23-7, Camiglibose 141200-24-0, Darglitazone 170861-63-9, JTT-501 199914-96-0 371968-35-3D, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzene compds. in combination therapy for diabetes and diabetes-related disorders)

=> d bib hit 7

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:754995 CAPLUS
DN 137:268473
TI Porous drug matrices and methods of manufacture thereof
IN Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PA Acusphere Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142050	A1	20021003	US 2002-53929	20020122
	US 6395300	B1	20020528	US 1999-433486	19991104
	EP 1642572	A1	20060405	EP 2005-27194	20000525
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CN 1823737	A	20060830	CN 2005-10136940	20000525
	US 6645528	B1	20031111	US 2000-694407	20001023
	US 6932983	B1	20050823	US 2000-706045	20001103

	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
	US 2005048116	A1	20050303	US 2004-924642	20040824
	US 2005058710	A1	20050317	US 2004-928886	20040827
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		
	US 1999-433486	A2	19991104		
	US 2000-186310P	P	20000302		
	CN 2000-808161	A3	20000525		
	EP 2000-939365	A3	20000525		
	US 2002-53929	A3	20020122		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 52-53-9, Verapamil 53-03-2, Prednisone 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 631-61-8, Ammonium acetate 657-24-9, Metformin 745-65-3, Alprostadil 846-49-1, Lorazepam 1066-33-7, Ammonium bicarbonate 1863-63-4, Ammonium benzoate 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9005-65-6, Tween 80 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12125-02-9, Ammonium chloride, biological studies 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 25322-68-3, Polyethylene glycol 26266-57-9, Span 40 27203-92-5, Tramadol 28860-95-9, Carbidopa

28981-97-7, Alprazolam. 29094-61-9, Glipizide 30516-87-1, Zidovudine
32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34911-55-2, Bupropion
36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4,
Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51333-22-3,
Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide
54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine
54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2,
Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 60142-96-3,
Gabapentin 60205-81-4, Ipratropium. 63659-18-7, Betaxolol
65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1,
Alendronate 66852-54-8, Halobetasol propionate 68693-11-8, Modafinil
69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride
72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime
72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole
75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril
76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6,
Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate
78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine
hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate
79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine
79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4,
Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir
82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril
83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7,
Mometasone furoate 84625-61-6, Itraconazole 86386-73-4, Fluconazole
86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril
87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 90566-53-3,
Fluticasone 91161-71-6, Terbinafine 91421-42-0, Rubitecan
93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4,
Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin
97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8,
Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6,
Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan
hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole
103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4,
Famciclovir 104632-25-9, Pramipexole dihydrochloride 106266-06-2,
Risperidone 106392-12-5, Pluronic f127 106463-17-6, Tamsulosin
hydrochloride 106685-40-9, Adapalene 107753-78-6, Zafirlukast
109889-09-0, Granisetron 110871-86-8, Sparfloxacin 111470-99-6,
Amlodipine besylate 111974-72-2, Quetiapine fumarate 112809-51-5,
Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan
114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4,
Donepezil 124832-26-4, Valacyclovir 127779-20-8, Saquinavir
131918-61-1, Paricalcitol 132539-06-1, Olanzapine 134308-13-7,
Tolcapone 134678-17-4, Lamivudine 137862-53-4, Valsartan
140678-14-4, Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride
144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil
147059-72-1, Trovafloxacin 147245-92-9, Glatiramer acetate
150378-17-9, Indinavir 154248-97-2, Imiglucerase 154598-52-4,
Efavirenz 155141-29-0, Rosiglitazone maleate 155213-67-5, Ritonavir
158966-92-8, Montelukast 159989-65-8, Nelfinavir mesylate 161814-49-9,
Amprenavir 162011-90-7, Rofecoxib 169590-42-5, Celecoxib
171599-83-0, Sildenafil citrate 260779-88-2, Cisapride monohydrate
679809-58-6, Enoxaparin sodium
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

=> d bib hit 6

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1020106 CAPLUS

DN 141:420397
TI Albumin binding sites for evaluating drug interactions, and methods for evaluating or designing drugs based on their albumin binding properties
IN Carter, Daniel C.; Ho, Joseph; Wang, Zhongmin
PA New Century Pharmaceuticals, USA
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004102151	A2	20041125	WO 2004-US14046	20040506
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2565308	A1	20041125	CA 2004-2565308	20040506
PRAI	US 2003-468057P	P	20030506		
	WO 2004-US14046	W	20040506		

AB A method is provided for evaluating drug compds. based on their binding properties to human serum albumin, wherein structural information at particular albumin binding regions is entered into a computer database and assessed with regard to particular contacting binding residues located in accordance with the invention. The information obtained through the computer database is thus useful in assessing and predicting drug interactions at albumin binding sites. Further, protein fragments including one or more albumin binding sites are provided which can be used in methods of assessing and designing drugs.

IT 50-28-2, Beta-Estradiol, biological studies 50-78-2, Aspirin 52-86-8, Haloperidol 53-03-2, Prednisone 53-86-1, Indomethacin 57-41-0, Phenytoin 57-63-6, Ethinyl-Estradiol 58-94-6, Chlorothiazide 60-87-7, Promethazine 61-33-6, Penicillin G, biological studies 61-68-7, Mefenamic Acid 81-82-3 86-54-4, Hydralazine 87-08-1, Penicillin V 94-20-2, Chlorpropamide 127-69-5, Sulfisoxazole 135-07-9, Methyclothiazide 302-79-4, Tretinoin 469-62-5, Propoxyphene 552-94-3, Salsalate 599-79-1, Sulfasalazine 604-75-1, Oxazepam 637-07-0, Clofibrate 644-62-2, Meclofenamic Acid 979-32-8, Estradiol Valerate 5104-49-4, Flurbiprofen 5543-58-8 7689-03-4, Camptothecin 10238-21-8, Glyburide 12650-69-0, Mupirocin 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16009-13-5, Hemin 19216-56-9, Prazosin 21256-18-8, Oxaprozin 22204-53-1, Naproxen 22494-42-4, Diflunisal 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 29767-20-2, Teniposide 34911-55-2, Bupropion 36322-90-4, Piroxicam 36505-84-7, Buspirone 38396-39-3, Bupivacaine 41340-25-4, Etodolac 41744-40-5, Sulbenicillin 42924-53-8, Nabumetone 51146-56-6, S-Ibuprofen 58957-92-9, Idarubicin 59729-33-8, Citalopram 63590-64-7, Terazosin 66635-92-5, S-Ketorolac 66635-93-6, R-Ketorolac 71125-38-7, Meloxicam 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 74103-06-3, Ketorolac 75330-75-5, Lovastatin 80573-04-2, Balsalazide 83366-66-9, Nefazodone 87226-41-3, R-Etodolac 87249-11-4, S-Etodolac 87333-19-5, Ramipril 90357-06-5, Bicalutamide 91161-71-6, Terbinafine 91421-42-0, 9 Nitro-Camptothecin 93957-54-1, Fluvastatin 102625-70-7, Pantoprazole 106266-06-2, Risperidone 107753-78-6, Zafirlukast 108605-62-5, A77 1726 111025-46-8, Pioglitazone 111470-99-6, Amlodipine Besylate 114798-26-4, Losartan

120014-06-4, Donepezil 144701-48-4, Telmisartan 145040-37-5, Candesartan Cilexetil 169590-42-5, Celecoxib 796061-49-9, NCP 007 796061-54-6, NCP 008 796061-55-7, NCP 012 796061-56-8, NCP 023 796061-57-9, NCP 024 796061-61-5, NCP 049 796061-65-9, NCP 051 796061-69-3, NCP 014
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(albumin binding sites for evaluating drug interactions, and methods for evaluating or designing drugs based on albumin binding properties)

=> d bib hit 5

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:638706 CAPLUS
DN 143:159548
TI Donepezil formulations
IN Boehm, Garth; Dundon, Josephine
PA Alpharma, Inc., USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005065645	A2	20050721	WO 2004-US42999	20041223
	WO 2005065645	A3	20051027		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2552221	A1	20050721	CA 2004-2552221	20041223
	US 2005232990	A1	20051020	US 2004-22346	20041223
	EP 1776089	A2	20070425	EP 2004-815115	20041223
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	IN 2006DN04397	A	20070713	IN 2006-DN4397	20060728
PRAI	US 2003-533496P	P	20031231		
	WO 2004-US42999	W	20041223		

AB Donepezil formulations, including amorphous donepezil or pharmaceutically acceptable salts thereof; sustained-release formulations; and donepezil sprinkle formulations are disclosed.
IT 120014-06-4, Donepezil
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(formulations)

=> d bib hit 1-4

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:385013 CAPLUS
DN 146:387123

TI Microparticles with modified release of at least one active principle and oral galenic form comprising same

IN Dargelas, Frederic; Guimberteau, Florence; Castan, Catherine; Meyrueix, Remi; Soula, Gerard

PA Flamel Technologies, Fr.

SO PCT Int. Appl., 50pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007036671	A2	20070405	WO 2006-FR50944	20060927
	WO 2007036671	A3	20070524		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	FR 2891459	A1	20070406	FR 2005-52985	20050930
PRAI	FR 2005-52985	A	20050930		

AB The invention concerns microparticle systems with modified release of oral active principle(s). The invention aims at providing a novel multimicroparticle galenic system operating in accordance with a dual time-dependent and pH-dependent release mechanism, which enables the following three parameters to be adjusted independently of one another: (a) the latent period preceding the release of the active principle in the stomach; (b) the pH triggering the release of the active principle in the intestine; (c) the release speed of the active principle. This is achieved through the use of coated microparticles made from particles of active principle each coated with two coating films A and B. Film A comprises: film-forming (co)polymer (A1) insol. in fluids of the gastrointestinal tract, Et cellulose (co)polymer (A2) soluble in fluids of the gastrointestinal tract, plasticizing polyvinylpyrrolidone (A3), and castor oil and optionally a surfactant and/or magnesium stearate lubricant (A4). Film B comprises a hydrophilic polymer (B1) bearing ionized groups with neutral pH (Eudragit L100-55) and a hydrophobic compound (B2) (Lubritab). Metformin hydrochloride and povidone were dissolved in water and spray-dried over neural microspheres. The microspheres were then coated to obtain prolonged-release metformin microparticles.

IT 88107-10-2, Tomelukast 88150-42-9, Amlodipine 88851-62-1, Piriprost potassium 88931-51-5, Clinprost 89365-50-4, Salmeterol 89565-68-4, Tropisetron 89667-40-3, Isbogrel 89778-26-7, Toremifene 90357-06-5, Bicalutamide 90566-53-3, Fluticasone= 91161-71-6, Terbinafine 91374-21-9 91832-40-5, Cefdinir 92623-85-3, Milnacipran= 92665-29-7, Cefprozil 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine= 93479-97-1, Glimepiride 93792-59-7, Hydroxypropyl methyl cellulose succinate 93957-54-1, Fluvastatin 94535-50-9, Levcromakalim 95058-81-4, Gemcitabine 95190-13-9, Tetrazolastmeglumine 95233-18-4, Atovaquone 95260-33-6, HYDROXYNORPETHIDINE 95634-82-5, Batelapine 96036-03-2, Meropenem 96566-25-5, Ablukast 96829-58-2, Orlistat 97048-13-0, Urofollitropin 97240-79-4, Topiramate 97322-87-7, Troglitazone 97466-90-5, Quinelorane 97519-39-6, Ceftibutene 97682-44-5, Irinotecan 97852-72-7, Tibenelast 97901-21-8, Nafagrel

98048-97-6, Fosinopril 98079-51-7 98116-53-1, Sulukast 98224-03-4, Eltoprazine 98319-26-7, Finasteride 98651-66-2, Halobetasol 99107-52-5, Bunaprolast 99614-02-5, Ondansetron 100927-14-8, Befiperide 100986-85-4, Levofloxacin 101001-34-7, Pamicogrel 101626-70-4, Talipexole 102625-70-7, Pantoprazole 102767-28-2, Levetiracetam 103177-37-3, Pranlukast 103577-45-3, Lansoprazole 103628-46-2, Sumatriptan 103775-10-6, Moexipril 103878-84-8, Lazabemide 103890-78-4, Lacidipine 104227-87-4, Famcyclovir 104363-98-6, Y20811 104632-26-0, Pramipexole 105462-24-6 105816-04-4, Nateglinide 105857-23-6, Activase 105920-77-2, Camonagrel 106266-06-2, Risperidone 106516-24-9, Sertindole= 106861-44-3, Mivacurium chloride 107023-41-6, Pobilukast 107266-06-8, Gevotroline 107266-08-0, Carvotroline 107753-78-6, Zafirlukast 107868-30-4, Exemestane 108778-82-1, Beractant 109889-09-0, Granisetron 110871-86-8, Sparfloxacin 111025-46-8, Pioglitazone 111406-87-2, Zileuton 111753-73-2, Satigrel 111974-60-8, Ritolukast 111974-69-7, Quetiapine 112362-50-2, Dalfopristin 112809-51-5, Letrozole 112811-59-3, Gatifloxacin 112887-68-0, Tomudex 112922-55-1, Cericlamine 112966-96-8, Domitroban 113665-84-2, Clopidogrel 113775-47-6, Dexmedetomidine 113852-37-2, Cidofovir 114798-26-4, Losartan 114977-28-5, Docetaxel 115103-54-3, Tiagabine 115256-11-6, Dofetilide 115956-12-2, Dolasetron 116539-59-4, Duloxetine 117976-89-3, Rabeprazole 118072-93-8, Zoledronate 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 119356-77-3, Dapoxetine 119386-96-8, Mofegiline 120014-06-4, Donepezil 120138-50-3, Quinupristin 120279-96-1, Dorzolamide 120443-16-5, Verlukast 120511-73-1, Anastrozole 120993-53-5, Desirudin 121679-13-8, Naratriptan 122320-73-4, Rosiglitazone 122647-31-8, Ibutilide 123039-93-0, Dihydrexidine 123308-22-5, Sezolamide 123441-03-2, Rivastigmine 123774-72-1, Sargramostim 123948-87-8, Topotecan 124832-26-4, Valacyclovir 124904-93-4, Ganirelix 125722-16-9, Enofelast 125926-17-2, Sarpogrelate 125935-84-4, Hylan 127779-20-8, Saquinavir 127943-53-7, Discodermolide 128312-51-6, Cinalukast 129029-23-8, Ocaperidone 129318-43-0 129497-78-5, Verteporfin 129618-40-2, Nevirapine 130018-77-8, Levocetirizine 130167-69-0, Pegaspargase 130209-82-4, Latanoprost 130929-57-6, Entacapone 131081-40-8, Silteplase 131741-08-7, Simendan 131796-63-9, Odapipam 131831-03-3, Sunipetron 132539-06-1, Olanzapine= 133040-01-4, Eprosartan 133454-47-4, Iloperidone 133652-38-7, Reteplase 133737-32-3, Pagoclone 133814-18-3, Doxacurium 134208-17-6, Mazapertine= 134308-13-7, Tolcapone 134523-00-5, Atorvastatin 134678-17-4, Lamivudine= 135062-02-1, Repaglinide 136236-51-6, Rasagiline 136470-78-5, Abacavir 136817-59-9, Delavirdine 137862-53-4, Valsartan= 138068-37-8, Lepirudin 138402-11-6, Irbesartan 139110-80-8, Zanamivir 139133-26-9, Lexipafant 139264-17-8, Zolmitriptan 139481-59-7, Candesartan 140942-13-8, Quinobene 141505-33-1, Levosimendan 142852-51-5, TAK-147 143322-58-1, Eletriptan 143558-00-3, Rocuronium 143653-53-6, Abciximab 144034-80-0, Rizatriptan 144412-49-7, Lamifiban 144494-65-5, Tirofiban 144598-75-4, Paliperidone 144701-48-4, Telmisartan 145508-78-7, CP118954 145599-86-6, Cerivastatin 146426-40-6, Flavopiridol 146939-27-7, Ziprasidone= 147059-72-1, Trovafloxacin 147432-77-7, Ontazolast 148396-36-5, Fradafiban 149503-79-7, Lefradafiban 149649-22-9, Nafadotride= 149820-74-6, Xemilofiban 150378-17-9, Indinavir 151319-34-5, Zaleplon 152923-56-3, Daclizumab= 153559-49-0, Bexarotene 154361-50-9, Capecitabine 154598-52-4, Efavirenz 155213-67-5, Ritonavir 158966-92-8, Montelukast 159776-70-2, Melagatran 159989-64-7, Nelfinavir= 161814-49-9, Amprenavir 162011-90-7, Rofecoxib 163250-90-6, Orbofiban 167933-07-5, Flibanserin 170277-31-3, Infliximab 171655-91-7, Brasofensine 171752-56-0, Adrogolide 173146-27-5, Denileukin diftitox 174722-31-7, Rituximab 179120-92-4, Altinicline 180288-69-1,

Trastuzumab 183325-78-2, Calfactant 188039-54-5, Palivizumab 188627-80-7, Eptifibatide 196618-13-0, Oseltamivir 218620-50-9, Pegvisomant 465499-11-0, Rapacuronium= 612534-95-9, Azithromycine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microparticles with modified release of at least one active principle and oral galenic form comprising same)

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:118095 CAPLUS
DN 146:190546
TI Gelled donepezil compositions containing oils and gelling agents for improved stability
IN Shudo, Jutaro; Yoneto, Kunio
PA USA
SO U.S. Pat. Appl. Publ., 9pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007026075	A1	20070201	US 2006-476410	20060627
WO 2007018801	A1	20070215	WO 2006-US25112	20060627

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-704104P P 20050728
IT Amorphophallus rivieri
Central nervous system agents
Gelation agents
Stability
Surfactants
pH
(gelled donepezil compns. containing oils and gelling agents for improved stability)
IT 50-70-4, D-Sorbitol, biological studies 94-13-3, Propyl p-hydroxybenzoate 110-27-0, Isopropyl myristate 128-44-9, Sodium Saccharine 151-21-3, Sodium lauryl sulfate, biological studies 621-71-6, Tricaprin 2624-31-9, Potassium palmitate 3234-81-9, Octadecyl myristate 4706-78-9, Potassium lauryl sulfate 8063-16-9, Psyllium seed gum 9000-01-5, Acacia gum 9000-07-1, Carrageenan 9000-28-6, Ghatti gum 9000-30-0, Guar gum 9000-36-6, Karaya gum 9000-40-2, Locust bean gum 9000-65-1, Tragacanth gum 9000-69-5, Pectin 9002-18-0, Agar 9002-89-5, Polyvinyl alcohol 9003-01-4, Polyacrylic acid 9003-04-7, Sodium polyacrylate 9003-11-6, Polyoxyethylene polyoxy propylene glycol 9003-39-8, Polyvinyl pyrrolidone 9004-32-4, Carmellose sodium 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs. 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9004-64-2, Hydroxypropyl cellulose 9004-67-5, Methyl cellulose 9005-27-0, Hydroxyethyl starch 9005-32-7, Alginic acid 9005-38-3, Sodium alginate 9012-76-4, Chitosan 9032-42-2, Hydroxyethyl methyl cellulose 9036-66-2, Arabinogalactan 9036-88-8, Mannan 9049-76-7, Hydroxypropyl starch 9057-02-7, Pullulan 9057-06-1, Carboxymethyl

starch 9062-07-1, ι-Carrageenan 11078-31-2, D-Gluco-D-mannan 11138-66-2, Xanthan gum 25086-89-9 25322-68-3, Macrogol 37220-17-0, Konjak mannan 39300-88-4, Tara gum 51434-18-5, Cassia gum 64366-24-1, Potassium-carrageenan 68797-35-3, Dipotassium glycyrrhizinate 71010-52-1, Gellan gum 120011-70-3, Donepezil hydrochloride 120014-06-4, Donepezil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gelled donepezil compns. containing oils and gelling agents for improved stability)

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:299138 CAPLUS
DN 144:338152
TI Use of purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride
IN Arad, Oded; Zelikovitch, Lior; Alnabari, Mohammed; Brand, Michael; Gribun, Irina; Salman, Ada; Shiffer, Meital; Shookrun, Moty; Kurlat, Orna; Bentolila, Moshe; Kaspi, Joseph
PA Israel
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006069125	A1	20060330	US 2005-235106	20050927
AU 2005288521	A1	20060406	AU 2005-288521	20050927
CA 2581926	A1	20060406	CA 2005-2581926	20050927
WO 2006035433	A2	20060406	WO 2005-IL1034	20050927
WO 2006035433	A3	20060727		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-613707P	P	20040929	
WO 2005-IL1034	W	20050927	

TI Use of purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride
AB The present invention provides a crystalline donepezil maleate, which is used as an intermediate in the preparation of donepezil hydrochloride. Also provided are novel processes for producing same in substantially pure form and a process for producing pharmaceutically pure amorphous donepezil hydrochloride therefrom.
IT Solvents
(organic; purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)
IT Crystallization
Freeze drying
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)
IT Disaccharides
Monosaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT Drying
(spray; purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 60-29-7, Diethyl ether, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 67-66-3, Chloroform, uses 71-23-8, Propanol, uses 71-36-3, Butanol, uses 75-05-8, Acetonitrile, uses 75-09-2, Dichloromethane, uses 78-92-2, sec-Butanol 78-93-3, Methylethyl ketone, uses 108-20-3, Diisopropyl ether 108-21-4, Isopropyl acetate 108-88-3, Toluene, uses 110-19-0, Isobutyl acetate 110-54-3, Hexane, uses 141-78-6, Ethyl acetate, uses 1330-20-7, Xylene, uses 1634-04-4, Methyl tert-butyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 110-16-7, Maleic acid, reactions 497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 1310-58-3, Potassium hydroxide, reactions 1310-73-2, Sodium hydroxide, reactions 7647-01-0, Hydrochloric acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 880490-66-4P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 120014-06-4, Donepezil
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 120011-70-3P, Donepezil hydrochloride
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

IT 63-42-3, Lactose 69-65-8, Mannitol 9004-34-6D, Cellulose, derivs. 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9005-25-8, Starch, biological studies 9050-36-6, Maltodextrin 64044-51-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purified donepezil maleate for preparing pharmaceutically pure amorphous donepezil hydrochloride)

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1292008 CAPLUS
DN 144:27610
TI Preparation of polymorphs of donepezil hydrochloride
IN Aher, Umesh P.; Tarur, Venkatasubramanian R.; Sathe, Dhananjay Govind; Naidu, Avinash Venkataraman; Sawant, Kamlesh Digambar
PA India
SO U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S. Ser. No. 72,169.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005272775	A1	20051208	US 2005-145202	20050603

US 7186842	B2	20070306		
US 6649765	B1	20031118	US 2003-365717	20030212
US 2004158070	A1	20040812	US 2003-714724	20031117
US 6953856	B2	20051011		
US 2005107613	A1	20050519	US 2004-879816	20040629
WO 2006011154	A1	20060202	WO 2004-IN227	20040728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1771416	A1	20070411	EP 2004-806738	20040728
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV				
US 2005288330	A1	20051229	US 2005-72169	20050304
US 2007123565	A1	20070531	US 2006-557764	20061108
PRAI US 2003-365717	A2	20030212		
US 2003-714724	A2	20031117		
US 2004-879816	A2	20040629		
WO 2004-IN227	A	20040728		
US 2005-72169	A2	20050304		
US 2005-145202	A1	20050603		

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention discloses a novel, stable polymorph of 1-benzyl-4[(5,6-dimethoxy-1-indanone)-2-yl]methylpiperidine-HCl (donepezil-HCl) (I). Further the present invention discloses a process for producing amorphous I and its polymorphic Form VI. Thus, I was prepared by the reaction of the free base with oxalic acid followed by treatment with HCl.

IT 120014-06-4, Donepezil
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of polymorphs of donepezil hydrochloride)